No. R. 178 **2 March 2012**

NATIONAL HEALTH ACT, 2003

REGULATIONS RELATING TO THE REGISTRATION OF MICROBIOLOGICAL LABORATORIES AND THE ACQUISITION, IMPORTATION, HANDLING, MAINTENANCE AND SUPPLY OF HUMAN PATHOGENS

The Minister of Health has, in terms of section 68 of the National Health Act, 2003, (Act No 61 of 2003), made the regulations in the Schedule.

SCHEDULE

DEFINITIONS

1. In these regulations any word or expression to which a meaning has been assigned in the act shall have such meaning and, unless the context otherwise indicates –

"biosafety code" means a code for classifying human pathogens into five categories in accordance with the relative risk or risks that a particular human pathogen or any manipulation thereof, may pose in causing human disease and the relative seriousness of such disease, as set out in Table 2, 3, 4 and *5* of the standards;

"BSL code" means laboratory biosafety level code;

"diagnostic specimen" means any human or animal material, including excreta, secreta, blood and its components, tissue or tissue fluids, that is to be used for the purpose of diagnosis, but does not include live infected animals;

"human pathogen" means —

(a) an infectious substance (b) the toxin of an infectious substance, or (c) any diagnostic specimen, vector or other material that contains, or that is reasonably suspected to contain an infectious substance or a toxin of an infectious substance;

"infectious substance" means — (a) a micro-organism, virus or parasite that is capable of causing human disease, or (b) an artificially produced hybrid or mutant micro-organism that contains genetic components of any micro-organism capable of causing human disease;

"laboratory biosafety level code or BSL Code" means a code for the classification of microbiological laboratories into four levels of containment of human pathogens to conduct the activities referred to in regulation 3(a) or (b) in respect of human pathogens with a specific biosafety code;

"microbiological laboratory" means a laboratory which handles human pathogens capable of colonising in humans, irrespective of whether or not the laboratory undertakes specific culture of such human pathogens or merely receives and handles tissue and other specimens potentially infected or infested which such human pathogens, and including laboratories which handle infected or infested, or potentially infected or infested, indigenous vectors of human pathogens, or exotic vector species irrespective of whether the are infected or infested;

"routine diagnostic specimen" means any biological specimen obtained routinely from patients for determination of the presence or not of human pathogens in order to identify, confirm or exclude infectious diseases in such patients, but excludes human pathogens with biosafety codes 3, 4 or 5;

"standards" means the Biosafety Standards for Microbiological Laboratories as determined by the Minister;

"toxin of an infectious substance" means a toxin capable of causing human disease;

Application of the regulations.

2. (1) These regulations apply to all microbiological laboratories which acquire, receive, import, handle, manipulate, maintain, store, culture or in any way process, issue or dispose of human pathogens so acquired, received or imported.

(2) These regulations do not apply to veterinary, agricultural or industrial laboratories which conduct the, activities referred to in regulation 3(a) or (b) in respect of animal pathogens, or toxins thereof, incapable of causing human disease.

Registration of laboratories and the issuing of permits

3. No person shall-

(a) acquire, receive or import human pathogens; or (b) handle, manipulate, maintain, store, culture or in any way process, issue or in any way dispose of human pathogens so acquired, received or imported, unless the person-

(i) is registered with the Department as a microbiological laboratory in terms of regulation 6(l)(a); (ii) is assigned a BSL code in terms of regulation 6(l)(a); (iii) is in possession of a permit issued in terms of regulation 6(1)(b) to conduct the activities referred to in paragraph (a) or (b) in respect of human pathogens in accordance with the BSL code of the laboratory indicated on the permit; and (iv) conducts any activity referred to in (a) or (b), as the case may be, in accordance with the provisions of these regulations and the standards.

4 (1) An application for registration of a microbiological laboratory must be submitted to the Director-General in Form 2 and 3, 4or 6, as the case may be, as provided for in the annexure.

(2) An application for a permit contemplated in regulation 3(b) (iii) must be submitted to the Director-General in Form I as provided for in the annexure.

(3) The applications referred to in sub-regulations (1) and (2) must be accompanied by an application fee as may be determined by the Director-General.

5 (1) When considering an application made in terms of regulation 4 the Director-General may require the applicant to furnish such further information and materials in respect of the application as the Director-General may deem necessary.

(2) The Director-General may direct a health officer to-

(i) inspect, at any reasonable time, the physical facilities, equipment, operational protocols, systems or manuals or any other documents related to the functioning of the laboratory; (ii) take samples of any of the human pathogens found in the laboratory for testing or analyses; or (iii) investigate any other aspect of the laboratory that may assist the Director-General in making a decision on the application.

(3) The health officer referred to in sub regulation (2) must submit a report to the Director-General of the findings of the inspection.

6 (1) After considering an application, the Director-General may with regard to an application for-

(a) registration, issue a registration certificate to the applicant concerned, indicating a specific BSL code which is applicable to that laboratory, and any conditions that he or she may determine; or

(b) permit, determine the biosafety code of the human pathogens in a particular instance for which the application is being made and issue a permit to the applicant concerned, indicating in respect of which human pathogens activities may be conducted.

(2) In the case an application or applications received for registration of more than one laboratory from a single applicant, the Director-General shall determine what constitutes a separate laboratory in each case for the purpose of registration.

(3) The Director-General may by notice in writing sent by registered mail to the applicant, refuse to issue a registration certificate or permit and stating the reasons for such a decision.

(4) A permit issued in terms of this regulation is valid for a period of 90 days from the date of issue and for a single acquisition, receipt or importation of human pathogens.

7. Notwithstanding regulation 6, a laboratory issued with a permit for human pathogens with biosafety codes 1 or 2, need not apply for a permit for each acquisition from within the Republic of the same type of human pathogen for which such laboratory has been issued with a permit.

8. A laboratory which imports human pathogens or to which a permit has been issued for human pathogens with biosafety codes 3, 4 or 5, must apply for a permit for each import or acquisition of human pathogens.

9. (1) A person who acquired or imported a human pathogen that belongs to biosafery code 3, 4 or 5 shall keep the pathogen in the laboratory located at the address indicated in the application for a permit and shall ensure that the human pathogen is used only for work carried out or directed by such person in that laboratory.

(2) A person who intends to transfer a human pathogen to another person shall submit an application in writing to the Director-General for such a transfer.

(3) The Director-General may grant or reject an application for the transfer of a human pathogen.

10. A permit is not required for activities in respect of routine diagnostic specimens which are to be examined for human pathogens for which the laboratory concerned has been registered and assigned with the appropriate BSL code.

11. The original certificate of registration must be displayed in a conspicuous place in the laboratory.

Transfer of human pathogens

12. (1) The acquisition of human pathogens resulting from a transfer shall only take place with the written consent of the person in charge of the supplying registered laboratory and that of the receiving registered laboratory.

(2) The supplying laboratory is responsible for ensuring that the receiving laboratory is registered and assigned the appropriate BSL code to receive the human pathogens transferred.

(3) Records in respect of transfers shall be preserved and produced by the person in charge of the laboratory on demand to the Director-General.

(4) The transfer of human pathogens must be accompanied by the relevant permit.

Importation of human pathogens

13. (1) No person shall receive or import a human pathogen that belongs to biosafety code 3, 4 or 5, unless-

(a) prior to shipment of the human pathogen, that person notifies the supplier that the outer container in which the human pathogen is transported must display clearly, on the outside surface of the container, the number of the permit issued and the following statement preceding that number:

"Human Pathogen — Permit Number"; and

(b) the original permit issued in respect of the human pathogens accompanies the consignment of such human pathogen and is attached to the outer container of such human pathogen.

(2) A person who arranges to transfer or import a human pathogen that belongs to biosafety code 3, 4 or 5 and does not receive it within 3 days after such date as may be reasonably expected in the circumstances, shall-

(a) notify Director-General that the person has not received the human pathogen; and

(b) forthwith take all reasonable measures to locate the human pathogen

Suspension or cancellation of registration or permit

14. (1) If the Director-General is of the opinion on the strength of an inspection report or recommendation by a health officer, or any other person designated by the Director-General, that there are reasonable grounds to suspect that-

(a) the premises or equipment used by the laboratory to which a permit was issued or registered are hazardous to health;

(b) the laboratory is not complying with these regulations or the standards,

the Director-General may serve a written notice on the laboratory instructing the laboratory to furnish reasons, at a place and time specified in such notice, why the registration or permit concerned must not be suspended or cancelled.

(2) The Director-General may, notwithstanding sub-regulation (1), suspend the registration or permit immediately if she or he is of the opinion that the hazard referred to in sub-regulation (1) constitutes an immediate danger to health or a contravention of these regulations.

(3) A notice referred to in sub-regulation (1) shall set out such particulars as are reasonably adequate to inform the laboratory why the revocation of registration or permit is necessary.

15. The suspension or revocation of a registration or permit or both the registration and permit in terms of this regulation shall have the effect that, from the date when it is served on the laboratory, no activities referred to in regulation 3 may be conducted in or upon the premises of the laboratory.

16. Where the Director-General is of the opinion that a condition that gave rise to the revocation of a registration or permit was rectified after such revocation, she or he may, upon written application, reinstate such registration or permit.

Appeals

17. A registered laboratory or a laboratory which has applied for registration or the issuing of a permit, may appeal in writing to the Minister against any decision of the Director-General made in terms of these regulations

18. An appeal in terms of regulation 17 shall be lodged within 14 days of the receipt of a notice of such decision by the laboratory, and shall clearly state -

(a) against which decision such appeal is lodged; and (b) the grounds of such appeal.

19. Any appeal in terms of these regulations shall be lodged with the Director-General, who shall submit it to the Minister together with his or her reasons for the decision appealed against.

20. The Minister may confirm, amend or set aside a decision of the Director- General in. terms of the provisions of these regulations and inform the laboratory in writing of his decision.

Offences and penalties

21. Any person who contravenes the provisions of these regulations shall be guilty of an offence and shall on conviction be liable to a fine or imprisonment for a period not exceeding 10 years or to both fine or imprisonment.

DR A MOTSOALEDI, MP

MINISTER OF HEALTH

DATE: 1/3/2012

FORM 1

DEPARTMENT OF HEALTH

APPLICATION FOR PERMIT TO ACQUIRE, IMPORT OR HANDLE HUMAN PATHOGENS

in terms of regulation 3 of the *Regulations Regarding the Registration of Microbiological Laboratories and the Acquisition, importation, Handling, Maintenance and Supply of Human Pathogens,*

No. R.... of 2012

TO BE COMPLETED IN BLOCK LETTERS BY LABORATORY SUPERVISOR.

Item 1: Registration number of laboratory

B	S	L												

(Leave the number blank if the laboratory is not registered and complete the necessary sections in Form 2)

Item 2: Name of laboratory or institution

Item 3: Postal address of laboratory or institution

City/Town		Code	

Item 4: Street address of laboratory where human pathogens will be maintained

City/Town		Code	

Item 5: Laboratory Supervisor

Name	
Qualifications	
Health Professions Council of SA Registration number[1]	
Relevant experience	
Telephone number (work)	
Telephone number (after hours)	

Item 6: Institution from which human pathogens are to be acquired or imported (supplier)

Name	
Postal address	

[1] Attach copy of registration certificate

City/Town		Code	
Country			

Item 7: Has the necessary clearance been obtained from the (Provide evidence, e.g. photocopy of letter, etc.)

Yes		No	

Item 8: **Consignment** of human pathogens

Expected date of arrival		Port of entry[2]	
Means of transport			

Item 9: List of human pathogens to be imported or otherwise acquired[3]

Human pathogen	**Purpose for which required**	**OFFCIAL USE**

Item 10: Additional information furnished by applicant[3]

I certify that the information given in this application is correct and complete in every respect.

Signed at ..... on this ..... day of ..... 20 .....

Signature of applicant .....

(Laboratory Supervisor)

[2] If human pathogens are imported
[3] Attach separate page if not sufficient space

FORM 2

DEPARTMENT OF HEALTH

APPLICATION FOR REGISTRATION OF A MICROBIOLOGOCAL LABORATORY

in terms of regulation 3 of the *Regulations Regarding the Registration of Microbiological Laboratories and the Acquisition, Importation, Handling, Maintenance and Supply of Human Pathogens, No. R.... of .....*

TO BE COMPLETED IN BLOCKLETTERS BY LABORATORY SUPERVISOR. THE RELEVANT FORM 3, 4, 5 OR 6 MUST ALSO BE COMPLETED.

Item 1: Name of laboratory or institution

Item 2: Postal address of laboratory or institution

City/Town		Code	

Item 3: Street address of laboratory to be registered

City/Town		Code	

Item 4: Laboratory Supervisor

Name	
Date of birth	
Qualifications	
Health Professions Council of SA registration number[1]	
Relevant experience	
Telephone number (work)	
Telephone number (after hours)	

Item 5: Owner(s) of laboratory

Name			
Postal address			
City/Town		Code	

[1] Attach copy of registration certificate

Item 6: Contact person for owner (if different person from owner)

Name			
Postal address			
City/Town		Code	

Item 7: Intended function(s) of the laboratory[2]

Item 8: Brief description of premises to be registered (Type of construction; numbers of rooms stating floor dimensions and intended function of each; type of equipment and number of each; insert sketch of floor plan with room dimensions)[2]

Item 9: Has the laboratory been registered with the Department of Trade and Industry?

Yes		No		If yes, please attach a copy of the registration certificate

I certify that the information given in this application is correct and complete in every respect.

Signed at ..... on this ..... day of ..... 20 .....

Signature of applicant .....(Laboratory Supervisor)

[2] Attach separate page if not sufficient space

BIOSAFETY STANDARDS FOR MICROBIOLOGICAL LABORATORIES

1. PRINCIPLES OF SIOSAFETY

1.1 The term "containment" is used in describing methods for managing parasites, infectious agents and infected or potentially infected animals, tissues or other materials in the laboratory environment where they are handled or maintained. The purpose of containment is to reduce exposure of laboratory workers, other persons and the outside environment to potentially hazardous agents.

1.2 primary containment, the protection of personnel and the immediate laboratory environment from exposure to parasitic or infectious agents is provided by good microbiological technique and the use of appropriate safety equipment.

1.3 Secondary containment, the protection of the external laboratory environment from exposure to parasites or infectious materials, is provided by a combination of facility design and operational practices. In some instances primary containment is of less importance than secondary containment e.g where work is done with agents which are not hazardous to humans, but which are of significance should they escape to the environment.

1.4 This document specifies four biosafety levels (BSLI, 2, 3 and 4) which consist of combinations of laboratory practices and techniques, safety equipment and laboratory facilities which are commensurate with the intended function of the laboratory and the nature of the infectious agents to be handled or maintained therein Specific metazoan parasites and infectious agents are assigned to one or more of five biosafety levels on the basis of the potential hazard which they constitute and of the intended laboratory procedure to which they will be subjected. A fifth category (BSL5) of parasite or infectious agent refers to certain exotic or eradicated parasites or infectious agents whose acquisition and maintenance is entirely proscribed or authorized in exceptional circumstances only. Work on recombinant DNA molecules or with radio-active isotopes is subject to separate control and is not dealt with in this document beyond insisting that laboratories conform

with the relevant requirements. Likewise, this document is concerned with biosafety in animal experiments and does not deal with quality of animal care or experimental design beyond insisting that these conform with all statutory, scientific and ethical requirements which are subject to separate control.

2. TYPICAL APPLICATIONS FOR WHICH THE FOUR RIO-SAFETY LEVELS ARE APPROPRIATE

2.1 Biosafety level I (BSLI)

BSL1 practices, safety equipment and facilities are those appropriate for secondary educational and undergraduate training and teaching laboratories and for other facilities working with defined and characterized strains of viable infectious agents not known to cause disease in healthy adult humans or not known to colonize in humans. *Bacillus* cereus, *Naegleria gruberi* and canine distemper virus (Snyder-Hill strain) are representative of those microorganisms assigned to BSLI. However, it should be remembered that many agents not ordinarily associated with disease processes or colonization in humans are opportunistic pathogens and may cause infection in the young, the aged and in immunodeficient or immunosuppressed individuals. Vaccine strains which have undergone multiple *in viva* passages should not a *priori* be considered avirulent.

2.2 Biosafety level 2 (BSL2)

BSL2 practices, safety equipment and facilities are those which are applicable to clinical, diagnostic, teaching and other facilities working with the broad spectrum of indigenous moderate-risk agents present in the community and associated with human disease of varying severity. Activities with low aerosol potential with these agents can be conducted on the open bench using good microbiological techniques. The hepatitis agents (hepatitis A, hepatitis B, hepatitis C), and the salmonellae are representative of microorganisms assigned to BSL2. Primary hazards to personnel working with these agents relate to accidental auto-inoculation or ingestion of infectious materials. Procedures with high aerosol potential may predictably and significantly increase the risk of exposure of personnel to infectious aerosols and must be conducted in primary containment equipment or devices.

2.3 Biosafety level 3 (85L3)

BSL3 practices, safety equipment and facilities are those which are applicable to clinical, diagnostic, teaching, research or production facilities working with indigenous or exotic agents

which may readily cause serious and potentially lethal infections, *Mycobacterium tuberculosis* when grown to bulk or inoculated into animals (see Section 6). Rift Valley fever virus and *Coxiella burnett/are* representative of microorganisms assigned to BSL3. Primary hazards to personnel working with these agents relate to auto-inoculation, ingestion and exposure to infectious aerosols.

2.4 Biosafety level 4 (BSL4)

BSL4 practices, safety equipment and facilities are those which are applicable to working with dangercus and exotic agents which pose a high individual risk of life-threatening disease, or which are potentially of great veterinary or agricultural significance. All manipulations of potentially infectious diagnostic materials isolates and naturally or experimentally infected animals pose a high risk of exposure and infection t0 laboratory personnel, or of escape of the infectious agent to the environment. Crimean-Congo haemorrhagic fever and foot and mouth disease of cattle are viruses representative of the microorganisms assigned to BSL4.

3. SUMMARY OF LABORATORY FACILITY DESIGN AND FUNCTIONS•

3.1 The basic laboratory

This Laboratory provides general space appropriate for work with defined viable agents which are not associated with disease processes in healthy adults or which do not colonize in humans. All activities are regularly conducted on the open bench using standard laboratory practices.

3.2 The containment laboratory

This laboratory provides general space appropriate for work with infectious agents or potentially infectious materials when the hazard levels are low and laboratory personnel can be adequately protected by standard laboratory practice. Work is commonly conducted on the open bench with certain operations confined to biological safety cabinets. Conventional laboratory designs are adequate. Areas known to be sources of general contamination such as animal rooms and waste staging areas should not be adjacent to media processing areas, tissue culture laboratories, or patient care activities. Public areas and general offices to which non-laboratory staff requires frequent access should be separated from spaces which primarily support laboratory functions.

3.3 The high containment laboratory

This laboratory has special engineering features which make it possible for laboratory workers to handle hazardous materials without endangering themselves, the community, or the environment. The unique features which distinguish this laboratory from the basic and containment laboratories

are the provisions for access control and a specialized ventilation system. This high containment laboratory may be an entire building or a single module or complex of modules within a building. In such cases, the laboratory is separated by a controlled access zone from areas open to the public and laboratory personnel from other areas.

3.4 The maximum containment laboratory

This laboratory has special engineering and containment features that will allow the safe conduct of activities involving infectious agents that are extremely hazardous to the laboratory worker or that may. cause serious epidemic disease. Although the maximum containment laboratory is generally a separate building, it can be constructed as an isolated area within a building. The distinguishing characteristic of the laboratory is the provision of secondary barriers to prevent hazardous materials from escaping into the environment. Such barriers include sealing of all openings into the laboratory and installing airlocks or liquid disinfectant barriers, a contiguous clothing- change and a shower room, a double door autoclave, a biowaste treatment system, a separate ventilation system, and a treatment system to decontaminate exhaust air.

4. BIOLOGICAL SAFETY CABINETS

4.1 The Class I biological safety cabinet is an open-fronted, negative-pressure, ventilated cabinet with a minimum inward face velocity of the working opening of at least 23 metres per minute. The exhaust air from the cabinet is filtered by a high efficiency particulate air (HEPA)1 filter- This cabinet may be used in three operational modes: with a full-width open front, with an installed front closure panel not equipped with gloves and with an installed front closure panel equipped with arm- length rubber gloves.

4.2 The Class II vertical laminar-flow biological cabinet is an open- fronted, ventilated cabinet with an average inward face velocity at the work opening of at least 23 metres per minute. This cabinet provides a high efficiency particulate air-filtered (HEPA), recirculated mass airflow within the work space. The exhaust air from the cabinet is also filtered by high efficiency particulate air(HEPA) filters.

Personnel protection provided by Class I and Class II cabinets is dependent on the inward airflow, since the face velocities are similar; they generally provide an equivalent level of personnel protection. The use of these cabinets alone, however, is not appropriate for containment of highest-risk infectious agents because aerosols may accidentally escape through the open front.

The use of a Class II cabinet in the microbiological laboratory offers the additional capability and advantage of protecting materials contained within it from extraneous airborne contaminants; this

capability is provided by the high efficiency particulate air filtered (HEPA) recirculated mass airflow within the work space.

4.3 The Class III cabinet is a totally enclosed ventilated cabinet of gas-tight construction. Operations within the Class III cabinet are conducted through attached rubber gloves. When in use, the Class III cabinet is maintained under negative air pressure of at least 12.5mm water gauge. Supply air is drawn into the cabinet through high efficiency particulate air (HEPA) filters installed in series. The exhaust fan of the Class III cabinet is separate from the exhaust fan in the facility's ventilation system and exhaust air is also high efficiency particulate air-filtered (HE PA).

The Class III cabinet provides the highest level of personnel and product protection. This protection is provided by the physical isolation of the space in which the infectious agent is maintained. When these cabinets are required, all procedures involving infectious agents are contained within them. Several Class III cabinets are therefore typically set up as an interconnected system. All equipment required by the laboratory activity, such as incubators, refrigerators, and centrifuges, must be an integral part of the cabinet system. Double-doored autoclaves, chemical dunk tanks, fumigation chambers or ultraviolet- irradiated airlocks are also attached to the cabinet system to allow safe introduction and removal of supplies and equipment.

4.4 Personnel protection equivalent to that provided by Class III cabinets can also be obtained with a personnel suit area and Class I or Class II cabinets. This area is one in which the laboratory worker is protected from a potentially contaminated environment by a one-piece positive pressure suit ventilated by a life-support system. This area is entered through an airlock fitted with airtight doors. A chemical shower is provided to decontaminate the surfaces of the suit as the worker leaves the areas- The exhaust air from the suit area is filtered by two high efficiency particulate air (HEPA) filter units installed in series.

BIOSAFETY STANDARDS FOR MICROBIOLOGICAL LABORATORIES

5. SUMMARY OF BIOSAFETY LEVELS FOR MICROBIOLOGICAL AND BIOMEDICAL LABORATORIES

Table 1

BITY		SAFETY Equipment	FACILITITES
BSL1	Standard micro- biological practices	None: primary contain- ment provided by adherence to standard laboratory practices during open bench operations	Basic laboratory
BSL2 •	BSL1 practices plus: protective gloves and coats when conducting procedures with infec- tious agents; deconta- mination of all infec- tious waste; limited access	Partial containment equip- ment (I.e. Class I or II biological safety cabinets) used to isolate mechanical and manipulative procedures that produce readily detectable aerosols	Containment laboratory
BSL3 .	BSL2 practices plus: special laboratory clothing; controlled access	Partial or total contain- ment equipment (class I. II or III biological safety cabinets) isolate all procedures that may produce aerosols	High containment laboratory
BSL4	BSLS practices plus: entrance through change room where street clothing removed and laboratory clothing donned; shower on exit; all waste decontaminated on exit from facility	Total containment equipment (i.e. Class III bio-logical safety cabinets) used to isolate all the procedures and operations involving infectious materials of partial containment equipment in combination with full body air-supplied, positive pressure personnel suit used for all procedures and activities	Maximum containment laboratory ..

6. BIOSAFETY CODES ASSIGNED TO PARASITIC AND INFECTIOUS AGENTS AND VECTORS OF HUMAN DISEASE

6.1 Explanation of Tables 2 to 5 6.1.1

In Tables 2 to 5 and Section 6.2 biosafety codes are assigned to parasitic and infectious agents and vectors of human disease. Codes 1 to 4 correspond to BSL1 to 4 as set out in Forms 3, 4, 5 and 6 in this document as being appropriate combinations of laboratory practices, safety equipment and facility design for handling and maintaining the agents or vectors concerned. Code 5 does not correspond to a particular biosafety level, but pertains to agents which may only be acquired in exceptional circumstances outlined in Section 6.1.8 below.

6.1.2 In many instances different biosafety codes are assigned to the same agent- This is because greater risk may be associated with handling larger volumes, greater concentrations or animals infected with the same agent

6.1.3 The lists are not intended to be exhaustive. In general, it can be accepted that free-living microorganisms not known to cause disease in or to colonize in humans? are assigned to biosafety code I BSLI laboratories may be given special permission to handle agents assigned to codes higher than I for teaching purposes.

6.I.4 With regard to parasitic or infectious agents assigned to codes higher than BSLI, the intention is to specify particularly agents which are known or are likely to occur in South Africa. Where possible, broad categories are specified, e.g. the category human enterovirus serotypes 1-72" includes the polio-viruses. Coxsackie A and B viruses, echoviruses and the most recent members of this group such as the agents of haemorrhagic conjunctivitis and hepatitis A

6.15 In many instances it is necessary to stipulate individual members of the group since they may differ with regard to biosafety requirements or known prevalence in South Africa. Many individual agents from the "International Catalogue for Arboviruses" are stipulated since they occur in South Africa or elsewhere in Africa, or are likely to be required here for identification of agents isolated in this country.

6.1.6 Important or particularly hazardous pathogens not known to occur in this country are also specified since identification would be needed urgently if an outbreak of these viruses were to occur here.

6.1.7 Zoonotic agents and selected important veterinary pathogens appear on the lists, but there has been no attempt to include the broad spectrum of non-zoonotic veterinary pathogens prevalent in this country

6.1.8 Agents which have been assigned to biosafety code 5 may be imported or otherwise acquired in exceptional circumstances only. Some are important human pathogens which have been eradicated or do not occur here, such as smallpox virus. Others, such as 8V40 virus, could contaminate vaccines. Most are extremely important animal pathogens which may only be acquired with the permission of the Director of Veterinary Services of the Department of Agricultural Economics and Marketing. Plant pathogens or parasites are not specified in this document and may only be acquired with the permission of the Director of Plant and Seed Control of the Department of Agricultural Economics and Marketing

Medical laboratories which intend to work with any veterinary or agricultural pathogens or parasites should ascertain from the above authorities whether or not there are current restrictions on work with the agents concerned, irrespective of whether or not the agents are assigned to code 5.

Once a laboratory has obtained permission to acquire a code 5 agent, the Director-General will assign a new biosafety code, ranging from 1 to 4, to that agent. The new code has relevance only to the handling of the agent in the particular laboratory concerned and the agent remains code 5 for all other laboratories unless a ruling t0 the contrary is made.

6.1.9 In instances where laboratories wish to acquire agents which are not included in Tables 2 to 5 and Section 6.2, the Director General shall make individual rulings on the biodiversity code assigned to the agents concerned.

It should be noted that the lists and the codes assigned to agents are subject to modification as dictated by changing circumstances and by the experience gained in applying the system.

6.1.I0 Symbols used in Tables 2 to 5

Laboratory function to be performed:

A Activities involve the use or manipulation of small quantities or low concentrations of cultures or other materials known or suspected of containing the agent, i.e. up to 2 litres of non-concentrated culture fluid or 10 per cent infected tissue suspension, or up to I 0m1 of culture which has been concentrated.

B Activities involve the use or manipulation of large quantities or high concentrations of cultures or other materials known or suspected of containing the agent, i.e. more than 2 litres of nonconcentrated culture fluid or 10 per cent infected tissue suspension, or more than 10 ml of culture which has been concentrated.

C Activities involve the use or manipulation or vertebrate animals with natural or induced infection with the agent.

Biosafety codes:

I Agent to be used or manipulated in compliance with BSL1 requirements.

2 Agent to be used or manipulated in compliance with BSL2 requirements.

3 Agent to be used or manipulated in compliance with BSL3 requirements.

4 Agent to be used or manipulated in compliance with BSL4 requirements.

5 Importation or other acquisition of the agent prescribed or authorized in exceptional circumstances only.

6.2 Prescribed biosafety codes for invertebrate vectors of parasitic or infectious agents of human disease

Indigenous invertebrate vectors of human disease which are infected or potentially infected with the parasitic or infectious agents which they transmit, are assigned to the biosafety codes which pertain to the relevant parasites or infectious agents in Tables 2 to 5.

Exotic vector species fall under BSL5 and are assigned to a new code, ranging from SSLI to 4, with respect only to laboratories which have been granted special permission to acquire and to perform studies with a particular species.

Work with non-infected indigenous invertebrate vectors of human disease is not subject to specific control, but such vectors must be housed and handled under secure conditions as described in Section 4 of Forms 3 to 6 if they are moved to areas where they do not already occur in nature,

7. IMMUNOPROPHYLAXIS

Additional protection of personnel at risk can be achieved through prophylactic vaccination. Each institution should devise its own written policy with regard to immunization and maintain records of all vaccinations performed.

It is recommended that personnel who handled human blood or blood products should be tested for immunity to hepatitis B and immunized if susceptible. Other vaccines for which the known effectiveness clearly outweighs possible adverse reactions, including for example vaccines against yellow fever, plague, rabies and poliomyelitis, may be considered for use in situations where there is deemed to be particular risk. All normal precautions should apply in carrying out such immunizations and the use of non-registered vaccines, such as that for Rift Valley fever, must be cleared with the Medicines Control Council.

The Director-General of the Department of Health may rule that the use of a particular vaccine makes it permissible to work with an infectious agent in a laboratory of lower biosafety rating than would normally be permitted. However, the potential exposure of non-immunized persons to infection, and the possible contamination of the environment, remain prime consideration in such instances.

8. SHIPMENT OF HUMAN PATHOGENS AND RELATED MATERIALS

Routine medical specimens or cultures assigned to BSLI and 2 and being transported to laboratories or between laboratories within South Africa by clinicians, pathologists or their delegates. e.g. messengers, are not subject to special restrictions but should be packed safely. Materials sent by mail or public transport should be packed in accordance with postal and transport requirements.

All materials containing, or potentially containing, agents assigned to BSL3, 4 and 5, as well as all infectious agents consigned within South Africa to external destinations, must be packaged and consigned in compliance with international requirements (see also Figures):

8.1 Briefly, the primary container (usually a sealed glass ampoule, tube or bottle) is wrapped in sufficient absorbent material (paper towels or tissues) to absorb the entire contents in the event of leakage.

8.2 The wrapped primary container is placed in a durable, leak-proof secondary container. This is preferably a leak-proof, rigid, screw-cap, metal or plastic container.8.3. The secondary container is placed in a similar tertiary container. If the material to be shipped is stable or has been freeze dried,

this tertiary container serves as the shipping container and is labeled with the address of the shipper and consignee. It also receives an etiologic or infectious agent label as per examples in Figures..... and..... available at airports. Parcels sent abroad must also have a customs declaration label- The import permit obtained from the consignee is placed in an envelope taped to the outside of the parcel where it is available to transport, customs and health officials.

The import permit issued in some countries, notably the USA, takes the form of a label which is attached to the outside of the parcel.

8.4 II unstable materials are being consigned in the wet or frozen state, the tertiary container must be placed in a suitable cold box (e.g. expanded polystyrene container) which contains sufficient cold packs or dry ice to maintain the agent at the desired temperature during the estimated duration of the journey.

The outer wrapping of the parcel is labeled as in Section 8.3 and, if necessary extra labels are added indicating which end of the parcel is to face upwards and that the parcel is to be kept refrigerated or frozen, and that the contents are fragile.

8.5 If specimens are sent by air, it may be necessary to complete a shipper's declaration of dangerous goods in addition to the air waybill.

8.6 Always inform the consignee of the means of transport and expected arrival times of the consignment.